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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/782,596

02/19/2004

Chen W. Liaw

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EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

05/28/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,596	LIAW ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/28/2008, 04/17/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/17/2008 has been entered. All pending claims are canceled. New claims 31-45 are added. Claims 31-45 are pending and under consideration.

Withdrawn Objections and/or Rejections

All the rejections and objections set forth in previous office action are made moot by canceled claims.

Information Disclosure Statement

The Information Disclosure Statements submitted on 04/17/2008 and 03/28/2008 have been considered. An initialed copy is attached to this office action.

Claim Rejections Under 35 U.S.C. §101

(i). 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

(ii). Claims 31-45 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 31-45 are drawn to a screening method comprising contacting a G protein-coupled receptor (GPCR) of SEQ ID NO: 20 or a variant of thereof with a candidate compound and determining whether said candidate compound inhibits or stimulates said GPCR. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a “real world” context of use for the claimed invention which does not require further research.

The specification discloses the hARE-2 polypeptide of SEQ ID NO: 20, a putative GPCR, which shares 53% sequence homology to GPR27 (Table A, page 8) and that the hARE-2 polypeptide is expressed in the left and right cerebellum and in the substantia nigra (Table 27, page 27). Nonetheless, the specification fails to disclose the ligand of the putative GPCR, fails to provide any sufficient information or evidence on the biological functions or activities of the hARE-2 polypeptide of SEQ ID NO: 20, and fails to disclose a patentable utility for the claimed invention.

First, the invention lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification’s disclosure of the properties of a material. The assertion that the

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hARE-2 polypeptide of SEQ ID NO: 20 has 53% sequence homology to GPR27 does not endow the hARE-2 polypeptide and the claimed invention with a specific and substantial utility due to the great diversity in structures and functions of the GPCR family (Ji et al., *J. Biol. Chem.* 273:17299-17302, 1998). The functions of a GPCR have to be determined experimentally. Therefore, even if the sequence analysis can place a GPCR into the GPCR family, such an assignment does not render a specific biological function and thus a well-established utility to the GPCR, as is the case here. It is noted that neither the instant disclosure nor the prior art teaches the specific biological functions of GPR27, which the hARE-2 polypeptide is compared with.

The state of the art is such that the biological functions of proteins are unpredictable solely based upon sequence homology. The prior art teaches that sequence-based methods for function prediction are inadequate (*Trends in Biotech* 18: 34-39, 2000). There are putative seven transmembrane molecules, which do not appear to be coupled to a G protein (Ji et al., *J. Biol. Chem.* 273:17299-17302, 1998; in particular, the 3rd paragraph of left column of page 17299). No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well-established for the claimed invention.

Secondly, the present invention does not have a specific and substantial utility, as exemplified below. The specification asserts, for example, that the human orphan GPCR can be used to screen candidate compounds as inverse agonists, agonists or

partial agonists (see, e.g., page 15). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a “real world” context of use. The disclosure fails to identify the ligand and the biological functions of the hARE-2 polypeptide. Clearly, further research would be required to determine the functions of the hARE-2 polypeptide. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.”

In summary, the present invention fails to satisfy the utility requirement under 35 U.S.C. 101.

(iii). Response to Applicants’ argument

From the bottom of page 4 to the first paragraph of page 6 of Applicants’ response, Applicants argue that the selective expression pattern of hARE-2 in cells of the substantia nigra allows for modulation of the intracellular levels of downstream signaling molecules selectively in those cells and thus the claimed methods can be used to identify compounds that modulate the intracellular levels of molecules that are directly implicated in the survival of those cells, i.e., the claimed method can be used to identify compounds that increase the “well-being” of substantia nigra cells.

Applicants’ argument has been fully considered, but is not deemed to be persuasive because the instant disclosure fails to disclose the specific biological activity of the

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hARE-2 of SEQ ID NO: 2 and a causal link between the hARE-2 and Parkinson's disease. Since the biological function of hARE-2 is not disclosed, the compound identified in the methods using hARE-2 does not have a specific and substantial utility. The use of compounds identified in the method in increasing the "well-being" of substantial nigra cells is a "throw-away" utility.

Beginning at the third paragraph of page 6 of Applicants' response, Applicants argue that the claimed screening methods can be employed to identify compounds that can be employed in the study, diagnosis and/or monitoring of Parkinson's disease.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the instant disclosure fails to disclose a causal or correlative link between the hARE-2 and Parkinson's disease and fails to disclose any compounds identified by the claimed methods can be used for the diagnosis and/or diagnosis of Parkinson's disease. Moreover, the use of a compound identified by the claimed method in the study of Parkinson's disease does not represent a specific and substantial utility because it requires further research to identify or reasonably confirm the biological function of the hARE-2 or any physiological significance and thus the compounds screen by the claimed methods.

At page 8 of Applicants' response, Applicants cite MPEP §2107.01 and argue that tools for studying and monitoring diseases are frequently used in medicine and therefore

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have clear utility. Applicants also argue that MPEP dictates that screening assays have a clear, specific and unquestinable utility.

Applicants' argument has been fully considred, but is not deemed to be persuasive because the instant claims are drawn to "a method of screening", not a tool for studying and monitoring any particular diseases. Moreover, MPEP does not state that all screening assays are useful in a patent sense. In other words, even if screening assays have a clear, specifc and unquestionable utility in analyzing compounds in a research setting, this utility does not represent a utility in a patent sense. In fact, MPEP 2107.01 clearly states that a method of assaying for or identifying a material that itself has no specific and/or substantial utility does not have a specific and/or substantial utility.

Claim Rejections Under 35 U.S.C. §112, 1st Paragraph due to lack of utility

Claims 31-45 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's argument regarding the utility of the claimed invention has been fully considered, but is not deemed to be persuasive for the reasons set forth in the preceding section.

Claim Rejections under 35 USC § 112, 1st paragraph, Written Description

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 31 and 34-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 31 and 34-45 are drawn to a method of screening comprising contacting a G protein-coupled receptor (GPCR) with a candidate compound and determining whether said candidate compound inhibits or stimulates said GPCR, wherein said GPCR is encoded by a nucleic acid capable of hybridizing under stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 19, wherein said stringent conditions comprise a wash in 0.1 X SSC at 65 °C, and wherein said GPCR is constitutively active. The claims do not require that the GPCR variant possess any

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particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature.

The instant disclosure of an isolated polypeptide of SEQ ID NO: 20 and its encoding nucleic acid molecule set forth in SEQ ID NO: 19 does not adequately support the scope of the genus recited in the claims, which encompasses a substantial variety of variants of the polypeptide of SEQ ID NO: 20. A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case, disclosure of a single species of GPCR polypeptide is not sufficient to support the genus of GPCR variants recited in the claims. Moreover, while disclosing the amino acid sequence of SEQ ID NO: 20, the instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the genus of polypeptides recited in the claims. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed polypeptides as being identical to those instantly recited.

Due to the breadth of the claimed genus and lack of the definitive structural or functional features of the recited genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the recited genus and thus the instantly claimed methods.

(iii). Response to Applicants' argument

Applicants argue that the claims of this case require not only a nucleic acid capable of hybridizing under stringent conditions to a known sequence, but also that the nucleic acid encodes a constitutively active GPCR. Applicants argue that a person of ordinary skill in the art at the time of filing would have known how to identify said G protein-coupled receptor as constitutively in the absence of further analysis of the hARE-2 protein or gene, such as by using a GTP γ S assay as described at page 11, lines 1-15 of the originally-filed application. Applicants cite case law and argue that claims of this case recite a genus of nucleic acids that remain hybridization to a known sequence under stringent conditions and thus the genus of nucleic acids recited in the claims are structurally similar and, as such, are adequately described.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, the claims do not require that the variant of polypeptide of SEQ ID NO: 2 possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature. The limitation, "wherein said GPCR is constitutively active", does not represent a meaningful functional limitation. Secondly,

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the claims do not recite highly stringent condition; instead they recite “stringent conditions”. Moreover, only the washing conditions are given, which would yield structurally and functionally unrelated polypeptides. Furthermore, the mere disclosure of SEQ ID NO: 20 is not sufficient to support the genus of recited in the claims. Accordingly, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the recited genus and thus the instantly claimed methods.

Claim Rejections under 35 USC § 112, 2nd paragraph

(i). The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(ii). Claims 31-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 31-45 are indefinite for the following reasons:

(1). Claims 31-41, 43, and 45 recite “determining whether said candidate compound inhibits or stimulates said GPCR”. It is unclear what activity of said GPCR is intended to be determined, rendering the claims indefinite.

(2). Claims 35 and 36 recite “determining whether said candidate compound is an agonist of said GPCR” or “determining whether said candidate compound is an inverse

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agonist of said GPCR". However, it is unclear from the steps of the methods how an agonist or inverse agonist of said receptor is determined.

(3). Claims 31-45 are indefinite because they recite "stringent conditions", however, only the washing conditions are given, leaving the hybridization conditions undefined.

(iii). Response to Applicants' argument

Applicants' argue that there is no indefiniteness in the scope of the genus of nucleic acids recited in the claims because the recited wash conditions necessarily retain only nucleic acids that bind under high stringency. Applicants' argument has been fully considered, but is not deemed to be persuasive because the claims recite "hybridizing under stringent conditions", however, only the washing conditions are given, leaving the hybridization conditions undefined. Since neither the specification nor the prior art defines the term unambiguously, the claims are indefinite.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE**

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FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/

Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.

May 21, 2008